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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICANT: A. JAMES MIXSON : ART UNIT: TO BE
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FOR: HISTIDINE COPOLYMER AND METHODS :
FOR USING SAME

Asst. Commissioner for Patents
Washington, DC 20231

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Barbara J. Miller
(Typed or printed name of person mailing paper or fee)


(Signature of person mailing paper or fee)

PRELIMINARY AMENDMENT

Sir:

Prior to fee calculation and examination, please amend the above-identified
application as follows.

IN THE CLAIMS

Please add the following new claims:

27. (New) A pharmaceutical agent delivery composition comprising:

a pharmaceutical agent;

a transport polymer in association with the pharmaceutical agent, the transport
polymer comprising a peptide characterized as having at least 10 amino acid residues,

wherein at least 10% of the amino acid residues are histidine and at least 10% of the amino acid residues are non-histidine, wherein the non-histidine residues are selected so as to tailor the transport polymer to the pharmaceutical agent and a method of association between the pharmaceutical agent and the transport polymer, and wherein the molecular structure of the peptide is selected from the group consisting of:

linear, with the proviso that:

- a. the entire sequence of said peptide cannot be described by the formula: $(XHHX)_n$, wherein H is histidine, X is a hydrophobic amino acid, and n is an integer greater than or equal to 4;
- b. the entire sequence of said peptide cannot be described by the formula: $(XHXH)_n$, wherein H is histidine, X is a hydrophobic amino acid, and n is an integer greater than or equal to 4; and
- c. said peptide does not comprise a hexa-peptide having the sequence His-His-His-His-His-His, unless at least 10% of the remaining amino acid residues of said peptide are histidine; and

branched, with a backbone of 1 or more amino acid residues and at least one branch of 1 or more amino acid residues covalently attached to a side-group of an amino acid residue of said backbone, with the proviso that each branch can consist of a single histidine residue only if the backbone does not consist solely of lysine residues; and

optionally, at least one intracellular delivery component associated with said transport polymer and/or said pharmaceutical agent.

28. (New) The pharmaceutical agent delivery composition of claim 27, wherein the pharmaceutical agent has an overall net negative charge, and wherein the method of association between the pharmaceutical agent and the transport polymer is non-covalent.

29. (New) The pharmaceutical agent delivery composition of claim 28, wherein the pharmaceutical agent comprises nucleic acid and wherein the non-histidine residues are each independently selected from the group consisting of amino acids with

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comprising at least one intracellular delivery component.

the intracellular delivery component comprises a lipid.

the lipid is a cationic lipid.

the molecular structure of the peptide is linear.

the molecular structure of the peptide is branched.

the pharmaceutical agent comprises a therapeutic agent selected from the group consisting of an antisense oligonucleotide, a ribozyme, an RNA-cleaving DNA oligonucleotide, an expression vector, and a combination of two or more of the above.

the therapeutic agent is an RNA-cleaving DNA oligonucleotide which targets VEGF receptor mRNA.

said peptide comprises a segment of amino acid residues selected from the group consisting of:

K-H-K-H-K-H-K-H-K-H (SEQ ID NO: 14),
 K-H-K-H-K-H-K-G-K-H-K-H-K (SEQ ID NO:1),
 K-H-K-H-K-H-K-G-K-H-K-H-K-H-K (SEQ ID NO:2),
 K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:3),
 K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K (SEQ ID NO:4),
 K-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-H-K-H-K (SEQ ID NO:5),
 K-K-H-H-H-K-H-H-H-K-K-H-H-H-K-H-H-H-K-K (SEQ ID NO:6),
 H-H-K-H-H-K-H-H-K-H-H-K-H-H-K (SEQ ID NO:15),
 K-K-H-K-H-K-H-K-H-K-G-K-H-K-H-K-H-K-H-K-K (SEQ ID NO:16),
 end-to-end repeats of one or more of the above sequences, and the reverse of any of the above sequences.

39. (New) The pharmaceutical agent delivery composition of claim 27, further comprising a transition metal.

40. (New) A method for delivering a pharmaceutical agent to the interior of a cell, said method comprising a step of contacting the cell with the pharmaceutical agent delivery composition of claim 27.

41. (New) The method of claim 40, wherein the pharmaceutical agent has an overall net negative charge, and wherein the method of association between the pharmaceutical agent and the transport polymer is non-covalent.

42. (New) The method of claim 41, wherein the pharmaceutical agent comprises nucleic acid and wherein the non-histidine residues are each independently selected from the group consisting of amino acids with a side-group that carries a positive charge at physiological pH and amino acids that are neutral at physiological pH.

43. (New) The method of claim 42, wherein the non-histidine residues are each independently selected from the group consisting of lysine and glycine.

44. (New) The method of claim 41, wherein the pharmaceutical agent delivery composition further comprises at least one intracellular delivery component, wherein the intracellular delivery component comprises a cationic lipid.

REMARKS

The applicants respectfully request that the Preliminary Amendment be entered prior to fee calculation and examination. Support for newly added claims 27-44 can be found in the application and in the original claims. Specifically, support for newly added claims 27 and 34-35 can be found in original claims 1 and 4 and pages 12-14 of the application. Support for newly added claims 28-30 can be found in the application between page 12, line 31 to page 13, line 24. Support for newly added claims 31-32 can be found in original claims 4-5. Support for newly added claim 33 can be found on page 15, line 15. Support for newly added claim 36 can be found in original claim 10 and in the application between page 16, lines 15-33. Support for newly added claim 37 can be found on page 30, lines 27-30 of the application. Support for newly added claims 38-39 can be found in original claims 3 and 6. Support for newly added claim 40 can be found in original claim 12. Support for newly added claims 41-44 can be found in the original claim 12 and pages 12-15 and 25-31 of the application. No new matter has been added.

Early and favorable action is respectfully requested.

If any questions arise in connection with this application, kindly contact the undersigned at (302) 658-9141.

Respectfully submitted,
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